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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,481	09/15/2000	Mark D. Fidock	PC10350AGPR	2752

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EXAMINER
SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/29/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/663,481	FIDOCK, MARK D.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 1899* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-16 and 19-27* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-12,14,16,19-22 and 24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13,15 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. ***Election***

Applicant's election with traverse of Group I (claims 1, 13, 15 & 21), in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Group I & II claims should be combined for examination, since (1) the amino acid sequence(s) of Group I and the nucleotide sequence of Group II are entirely reflective of one another. As such, any search relevant to one would also perform the task of searching for the other.

This is not found persuasive because depending upon the restricted group (I or II) being examined, additional classes/subclasses have to be searched. For example, Group II claims, drawn to nucleic acid encoding a phosphodiesterase, vector , host cell and a method of making the protein, will involve searching for additional class 536 & subclass 23.2 for DNA encoding the enzyme; host cell (class 435, subclass 252.3) & vector (class 435, subclass 320.1) as compared to Group I claims, drawn to a phosphodiesterase, will involve searching for only class 435 & subclass 196. This additional searching as explained above would therefore involve undue burden to the Examiner.

Further each of the proteins and the encoding nucleic acid are structurally distinct (requiring a separate sequence search for each of the sequences) and have a different level of enzymatic activity.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 2-4, 6-12, 14, 16, 19-22 & 24-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 9.

5. Preliminary amendment filed 9.15.00 (Paper No. 4) cancelled claims 5, 17-18 & 23.

6. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in United Kingdom on 9.17.99.

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. Group I (claims 1, 13, 15 & 21) pertaining to SEQ ID NO : 1 are under consideration in this examination.

9. ***Claim Rejections - 35 U.S.C. § 112*** (first paragraph)

Deposit Requirement

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete

deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claim 15 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

While deposit of NCIMB Number 41026 have been made in accordance Budapest Treaty at a recognized depository; however, an affidavit or declaration [under 37 CFR 1.808] stating that : all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, the deposit will be maintained in a public depository for a period of 30 years, or 5

years after the last request or for the enforceable life of the patent, whichever is longer, and the deposit will be replaced if it should ever become inviable.

A statement under 37 CFR 1.808 is required to overcome this rejection.

10. ***Enablement***

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated phosphodiesterase of SEQ ID NO: 1, does not reasonably provide enablement for any variant, fragment, homolog or derivative thereof of SEQ ID NO : 1 (claim 1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 1 encompasses any variant, fragment, homolog or derivative thereof – pertaining to SEQ ID NO : 1 which may or may not have phosphodiesterase activity. The scope of the claim does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins fragments or amino acid sequences with or without phosphodiesterase activity broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of PDE.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The specification does not support the broad scope of the claim which encompass any amount of protein modifications of SEQ ID No: 1, which may now result in a protein totally diverse and functionally non-relevant to the original sequence because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting PDE activity; (B) the general tolerance of PDE to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any PDE residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Further, the phosphodiesterases/proteins from different sources having varying substrate specificities for cAMP or cGMP and the PDE activity in some tissues could be activated by calcium or calmodulin. Therefore, random modifications of the SEQ ID NO : 1 or the fragments or derivatives thereof, without adequate guidance, may result in a protein with no or entirely diverse PDE activity with different substrate specificity and cofactor requirement.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope

of the claims broadly including PDE with an enormous number of amino acid modifications of the PDE of SEQ ID No: 1 and retain PDE activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of PDE having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

11. ***35 U.S.C. § 112, first paragraph (Written Description)***

Claims 1, 13 & 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1, 13 & 21 recite 'variant, homologue, fragment or derivative of SEQ ID NO : 1. However, no variant, homologue or derivative of SEQ ID NO : 1 is given in the specification.

The specification, however, only provides a single representative species in the sequence of SEQ ID NO : 1. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species or modify the sequence(s) of SEQ ID Nos :1 by substitution, deletion or addition or make a polypeptide of an unknown activity. The specification also fails to describe additional representative species of SEQ ID NO : 1, viz., the variants, homologs or fragments such peptides by any activity other than the identifying structural characteristics recited in SEQ ID NO : 1, for which no predictability of activity is

apparent. Given this lack of additional representative species, such as the modifications in order to create a variant, homologue, fragment or derivative thereof and still have some activity and/or utility, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

12. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claims 13, 15 & 21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 15 & 21 recite abbreviations 'PDE or PDE1B2'. Claim 15 also recites 'expressable'.

The claims are unclear because the abbreviations remain undefined. The first use of uncommon abbreviations such as those recited in the claims be spelt out, which may be subsequently abbreviated.

The recitation 'expressable' in claim 15 is unclear in a grammatical sense. Substituting 'expressed' for 'expressable', or other suitable expression will overcome this rejection.

13. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1, 13 & 15 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 1, 13 & 15 to recite wording such as "An isolated amino acid sequence or isolated PDE ".

14. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 13 & 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Epstein [USP 5,885,834, 1997]. Epstein teaches a cyclic nucleotide phosphodiesterase (PDE) amino acid sequence of SEQ ID NO : 2, which is 96.5% identical to Applicants SEQ ID NO : 1. Since the claims are drawn to any variant or homolog or fragment of the sequence of SEQ ID NO : 1, with no limitation about the extent of the modifications reads on claim 1; and antibodies raised against the disclosed PDE will have a immunological reaction with an antibody raised against SEQ ID NO : 1, in view of the

close sequence homology (claim 13). Applicants' claim 21 recites a recombinant PDE1B2, which is an arbitrarily assigned number having phosphodiesterase activity, is therefore anticipated by any PDE, including a highly homologous sequence such as that disclosed by Epstein.

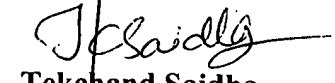
15. Claims 1, 13 & 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Beavo et al. [USP 5,389,834, 1995]. Beavo et al. teach a cyclic nucleotide phosphodiesterase (PDE) amino acid sequence of SEQ ID NO : 27, which is 92.8% identical to Applicants SEQ ID NO : 1. Since the claims are drawn to any variant or homolog or fragment of the sequence of SEQ ID NO : 1, with no limitation about the extent of the modifications (claim 1); and antibodies raised against the disclosed PDE will have a immunological reaction with an antibody raised against SEQ ID NO : 1, in view of the close sequence homology (claim 13). Applicants' claim 21 recites a recombinant PDE1B2, which is an arbitrarily assigned number having phosphodiesterase activity, is therefore anticipated by any PDE, including a highly homologous sequence such as that disclosed by Beavo et al..

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
August 27, 2003